



RESEARCH ARTICLE

TO STUDY EFFICACY AND SAFETY OF ADDITION OF INTRATHECAL CLONIDINE AND MIDAZOLAM TO HYPERBARIC BUPIVACAINE ADDED AS AN ADJUVANT FOR POST OPERATIVE ANALGESIA

*Piyush Kumar Sengar, Smita Priyadarshini and Piyush Setu

Department of Anesthesiology, Patliputra Medical College Hospital, Dhanbad - 826001

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ABSTRACT

Introduction: We compared the effects of addition of intrathecal clonidine and midazolam to 0.5% hyperbaric bupivacaine in terms of efficacy of sensory and motor block achieved and observed the side effects if any.

Methods: Forty patients of ASA Grade I and II between 18 – 60 years age of either sex undergoing lower limb surgeries were randomly allocated to any of the groups of 20 each by lottery method. Group M: Patients received Midazolam 2.5 mg preservative free (0.5 ml). Group C: Patients received Clonidine 75 micrograms (0.5 ml). These drugs were given with bupivacaine 15 mg (3 ml of 0.5 % hyperbaric solution) intrathecally. The time of onset, peak sensory and motor, 2 segment regression, time of rescue analgesia, haemodynamic changes and any other side effect were recorded.

Results: The motor blockade was significantly prolonged in group C (809.56 ± 290.38) than group M (533.80 ± 164.91). Two segment sensory regression, motor regression and time of rescue analgesia in group C (110.44 ± 28.77, 411.11 ± 82.07, 8.69 ± 0.92) was significantly more as compared to group M (66.10 ± 10.15, 159.80 ± 35.28, 4.28 ± 0.7) suggesting prolonged analgesia in intra-op & post-op periods.

Conclusion: 75 micrograms clonidine when added to 0.5% hyperbaric bupivacaine prolongs the sensory and motor block and reduces requirement of rescue analgesia as compared to 2.5mg midazolam.

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INTRODUCTION

Pain is not just sensory modality but is an experience¹. The international association for the study of pain defines pain as "an unpleasant sensory or emotional experience associated with actual or potential tissue damage in terms of such damage²". Many drugs opioids and nonopioids have been tried as an adjuvants to local anaesthetic agents used intrathecally³, not only to potentiate and increase the duration of block but also to provide good long lasting analgesia thus providing any untoward complications that may appear due to pain. Clonidine produces effective analgesia in postoperative patients⁴. The agonist action of clonidine on alpha 2 adrenergic receptors of spinal cord are responsible for its analgesic effect^{5,6}. Clonidine does not have respiratory depressant effect⁷ and also incidence of pruritus and vomiting are less frequent. Clonidine as an adjuvant also reduce the incidence of postanaesthetic shivering⁸.

Midazolam, an imidobenzodiazepine has been used as an adjuvant to bupivacaine for prolongation of analgesic effect in lower limb surgeries⁹. It also reduces the incidence of nausea and vomiting¹⁰. The goal of postoperative pain management is to reduce an individual patient's pain to a tolerable level with minimal or no associated suffering or distress¹¹. Successful outcome is the most desirable end point of any surgical procedure¹². Therefore anaesthetic and analgesic technique should aim not only to provide optimal conditions surgery but also to reduce postoperative morbidity and mortality¹³.

MATERIALS AND METHODS

The study was conducted at Patliputra Medical College and Hospital. After getting IEC clearance and taken written informed consent 40 patients of ASA grade I and II undergoing lower limb surgeries in the age group 18- 60 years were randomly allocated in 2 groups by lottery method. All the patients not willing to get enrolled in the study, not willing for spinal anaesthesia, age below 18 years and above 60 years, patients having previous history of allergies especially to

*Corresponding author: Piyush Kumar Sengar

Department of Anesthesiology, Patliputra Medical College Hospital, Dhanbad - 826001

benzodiazepines and adrenergic alpha 2 agonists, patients with local skin infections overlying lumbar vertebral region, patients with bleeding and /or coagulation disorders, patients with abnormal physiological profile were excluded from the study.

Group I: Patients were administered Midazolam 2.5 mg preservative free (0.5 ml) + bupivacaine 15 mg (3 ml of 0.5 % hyperbaric solution).

Group II: Patients were administered Clonidine 75 micrograms (0.5 ml) intrathecally + bupivacaine 15 mg (3 ml of 0.5 % hyperbaric solution) intrathecally.

Vital parameters like P.R, B.P, E.C.G, R.R, was recorded at interval of 3 minutes. The level of sensory blockade was tested by pin prick test until it reaches T5-T6 level, the motor blockade by Bromage scale and then surgical incision was allowed. The following readings was noted for assessment of onset of block T₀: Time of spinal anaesthesia T₁: time of onset of sensory block T₂: Time of onset of motor block. During surgery – complication of spinal anaesthesia was treated as following: - Hypotension: - Head low position upto 15 – 30 degrees, Rapid Infusion of fluids upto 100 ml- Vasopressors, ephedrine 2-6 mg , Mephenteramine 6 mg upto 30 mg max, Dopamine, Bradycardia -inj atropine 0.6 mg given. Respiratory discomfort - oxygenation and IPPV required Nausea and vomiting - correct hypotension inj.ondansetron 4 mg. Apprehension and anxiety – calm the patient. At the end of procedure patient were shifted to the recovery room and monitored for vital signs and VAS every 15 minutes for 1st hour and then every 30 minutes for vital signs and thereafter. Postoperative pain will be assessed by: 1. Visual analogue scale (VAS), Verbal numeral rating scale [The analysis was done by SPSS software version 11 by using percentage unpaired 't' test]. 'P' value less than 0.05 is considered as significant.

shown in Figure 1, which was statically significant with P value < 0.001 , P value <0.05, P value <0.05 respectively. There was slight fall in systolic blood pressure at 1min (119.11 ± 20.13) with F value of 4 and 5 min (114.22 ± 15.67) with F value of 8 in the clonidine group which was statistically significant with P value< 0.001 and P value <0.001 respectively as shown in figure 2. It was clinically significant and required intervention but was manageable.

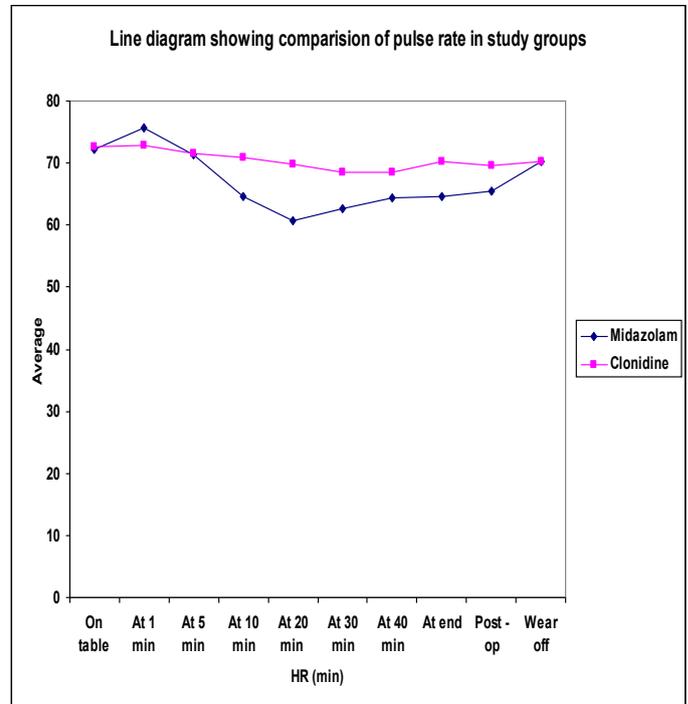


Figure 1.

No significant difference was found in diastolic blood pressure, SPO₂, respiratory rate, onset of motor and sensory blockade.

Table 1. Comparison of age in study groups

Parameters	Midazolam	Clonidine	t Value	P Value
	Mean ± SD (n=10)	Mean ± SD (n=10)		
Age (Yrs)	48.50 ± 8.51	34 ± 14.89	2.67	<0.01

Table 2. Comparison of total duration of motor blockade in study groups

Motor blockade	Midazolam	Clonidine	t Value	P Value
	Mean ± SD (n=10)	Mean ± SD (n=10)		
Total (Hrs)	2.65 ± 0.59	6.85 ± 1.37	8.90	<0.0001

Table 3. Comparison of total duration of analgesia in study groups

Analgesia	Midazolam	Clonidine	t Value	P Value
	Mean ± SD (n=10)	Mean ± SD (n=10)		
Total (Hrs)	4.28 ± 0.7	8.69 ± 0.92	13.13	<0.0001

RESULTS

There was no significant difference in the demographic data (age) as shown in Table 1. There was significant bradycardia in midazolam group in 20 min (60.80 ± 8.44) and the F value of 15.79 , 30 min (62.70 ± 6.98) and the F value of 13 and at end of procedure (64.70 ± 4.19) and the F value of 10 was as

The peak action, weaning off and total duration of sensory and motor blockade was more in clonidine group. The total duration of motor blockade was significantly longer in the clonidine group (p<0.05) as compared to midazolam group. The total duration of analgesia compared using VAS score was more in clonidine group shown in table 3. Clonidine significantly prolongs postoperative analgesia as compared to

midazolam although it causes mild transient hypotension and bradycardia. So, we conclude clonidine is a better adjuvant for spinal anaesthesia as compared to midazolam.

using midazolam used intrathecally and they found good results at reduced doses of 1 mg^{19,20} but did not found bradycardia which was found in our study.

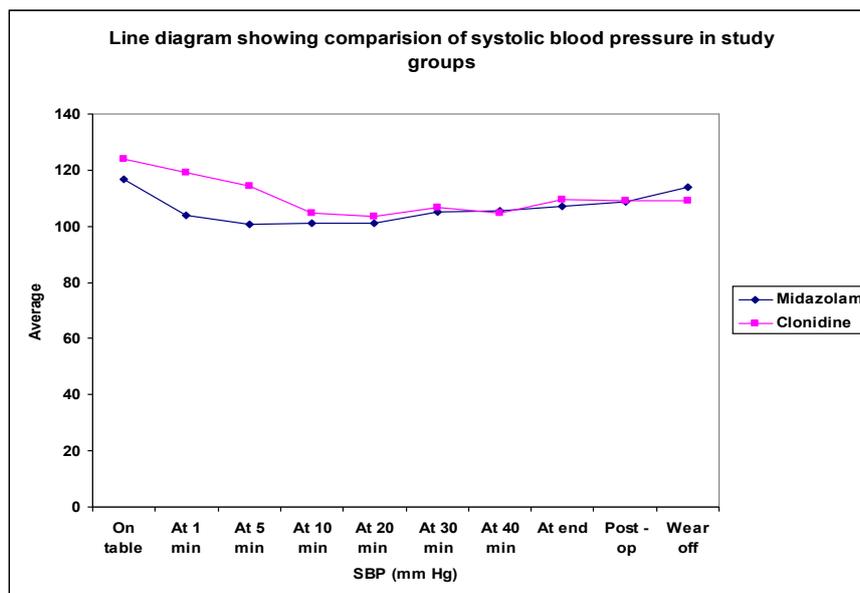


Figure 2.

DISCUSSION

Our data indicates that in spinal anaesthesia the addition of Clonidine 75 mcg or Midazolam 2.5 mg to hyperbaric bupivacaine (0.5 %) 3 ml prolongs the duration of analgesia (Table 3). The addition of either of the drugs prolongs the duration of analgesia and reduces the strain of postoperative care. Previously studies have been done by Karchana, P deepanjali, S jayshree using Intrathecal clonidine as an adjuvant to caudal analgesia in children¹⁴ has been done with clonidine 0.75 ml /kg of bupivacaine with clonidine 2 mcg/kg and got the prolonged analgesia. P. Lena, N. Balarac, J. J. Arnulf in coronary artery bypass grafting surgery clonidine 1 mcg/kg along with intrathecal morphine¹⁵ 4 mcg / kg given intrathecally before general anaesthesia and they found early extubation and good pain relief .Jellish WS, Abodeely A, Fluder EM, Shea J used Clonidine 150 mcg epidurally in patients undergoing laminectomy¹⁶ at the incision site and found prolonged analgesia. Our experience with clonidine was same and consistent with the results obtained from other studies where clonidine was used in orthopaedic surgeries¹⁷ clonidine was used < 150 mcg have prolonged sensory blockade along with bupivacaine 18 mg. Some studies in our group have the hypotension which was early manageable by routine and standard methods.

We does not observed any clinically significant bradycardia or retention of urine in our clonidine group and any sedation which was finded in our midazolam group. The study have done previously using clonidine in oral preparation and intrathecally but no prolongation of analgesia was in oral and subarachnoid with 150 mcg found profound analgesia¹⁸ by Bonnet F, Buisson VB, Francois Y .Clonidine used in our cases does not have reported any retention of urine. The studies have been done by TalwarVandana, RaiAnutam, Gandhi Radhika and Agarwal Nidhi, Usmani A., Sehgal R

In our groups clonidine takes more time to regress and have prolonged analgesia which is shown in our study. The patients administered clonidine has a much prolonged duration of analgesia. This combination of clonidine along with bupivacaine is best alternative to have pain free intraoperative and postoperative period with low cost proves it as a best adjuvant in present times.

Conclusion

The addition of clonidine to bupivacaine may be suitable and better alternative. We conclude that addition of 75 mcg clonidine to 0.5% hyperbaric bupivacaine prolongs motor and sensory block.

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